REMARKS

Claims 1, 2 and 5-20 were pending. Claim 1 is amended to use alternative language to encompass the intended subject matter. Support for the amendments are found throughout the specification at, *inter alia*, the original claims. New claim 21 has been introduced and is supported at least by original claim 11. No new matter has been introduced, and entry of the above revised claims is respectfully requested. Claims 1, 2 and 5-21 are pending. No claim is allowed.

Rejection Under 35 U.S.C. § 103(a)

Claims 1, 2, 5-12, 14-18 and 20 are rejected as allegedly being unpatentable over TAP Report 1 (Arch. Opthalmol. 117:1329-45 (1999). According to the Examiner, the TAP report teaches methods of administering verteporfin, a green porphyrin, to patient suffering from occult CNV. The Examiner asserts that patients receiving verteporfin had evidence of occult CNV with a visual acuity of less than 65 and a lesion size of less than 6 disc areas. The Examiner acknowledges that patients in the verteporfin arm of the study are not disclosed as having an occult component of at least about 50% to 100% of the lesion. According to the Examiner, it is obvious to treat patients with occult CNV lesions having an occult component of at least about 50% to 100% of the lesion. Claims 1-2 and 5-20 are rejected as allegedly being unpatentable over the TAP report in view of Zeimer (U.S. Patent No. 5, 925,942). Applicants traverse these rejections.

Applicants respectfully submit that the TAP Report 1 fails to render the claimed methods obvious because the TAP Report 1 fails to teach or suggest patients can successfully be treated with the claimed photodynamic therapy (PDT) methods if the patient having the claimed features, i.e., having a lesion having an occult component comprising greater than 50 and less than 100% *and* having a small lesion with a size less than 5 disc areas; having a lesion having an occult component comprising greater than 50 and less than 100% *and* poor visual acuity of less than 65 letters prior to treatment; or having a lesion having an occult component comprising greater than 50 and less than 100% and having a small lesion with a size less than 5 disc areas as well as poor visual acuity of less than 65 letters prior to treatment.

The TAP Report 1 describes a patient population with CNV and its treatment with verteporfin or placebo. Applicants begin by noting that a CNV lesion is composed of occult,

classical or some combination of occult and classical lesions. Alternately stated, whatever portion of a CNV lesion that is classical CNV, the remaining portion of the lesion is occult CNV. *See, e.g.*, the specification at page 2 and Exhibit 1 (QLT webpage). This explanation of the terminology informs the discussion of the results shown in the TAP Report 1.

The TAP Report 1 expressly teaches that there is no reasonable expectation of success in using PDT to treat patient having the features claimed in the instant methods. The TAP Report 1 explicitly teaches that patients with greater than 50% to less than 100% occult component in the CNV lesions (*i.e.*, >0 to <50% classical CNV) achieve **no benefit** from verteporfin PDT therapy. For example, in Table 5 on page 1340 of the TAP Report 1, there was no significant difference between verteporfin-treated patients and placebo-treatment group twelve months after treatment for the group of patients having a classical lesion >0 to <50 (*i.e.*, an occult lesion of >50 to <100%)[1]. According to the data shown in Table 5, 202 patients with a classical lesion >0 to <50 (*i.e.*, an occult lesion of >50 to <100%) were treated with verteporfin while 103 patients with the same lesion profile received placebo. A virtually identical percentage of patients in both groups experienced a loss of less than 15 letters in their visual acuity (55.9% with verteporfin treatment v. 55.3% placebo, p=0.92). In contrast, patients with ≥50% classical lesion (*i.e.*, ≤50% occult lesion), verteporfin significantly increased the number of patients with a loss of less than 15 letters compare with placebo treatment (67.3% v. 39.3%, p<.001, respectively). This suggests that verteporfin has *no effect* beyond that of the placebo in patients having lesions that are >50 to less than 100% occult, a conclusion also reached by the authors of the TAP Report 1. According to the report's authors,

> [no] **appreciable difference** was observed in the group of patients with lesions in which the area of classic CNV was greater than 0% but less than 50% of the area of the entire lesion at baseline.

See id. at page 1339, second column (emphasis added).

In describing the data relating to patients with *any* evidence of occult CNV, the authors note

[1] Applicants note that in the response filed on November 17, 2006 that the population of patients having >0 and <50% classical CNV (*i.e.*, >50-100% occult) was mistakenly referred to as having an occult lesion >0 and <50% (see page 4, last paragraph). Applicants regret the error and any confusion this may have caused in understanding the results of the TAP Report 1.

> [with] respect to eyes with evidence of occult CNV at study entry, **no major differences** were noted between verteporfin and placebo groups ... Progression of occult CNV was noted in 72% of eyes treated with verteporfin compared with 80% of eyes given placebo at month 12.

See the TAP Report 1 at page 1337, second column (emphasis added). In other words, verteporfin did not appear to affect progression of disease any more than the placebo did. This conclusion is stated again in the conclusion, where the authors assert that

> ... the lesion composition affected the magnitude of treatment benefit to a statistically significant degree. Predominantly classic CNV lesions (in which the area of classic CNV was ≥50% of the area of the entire lesion at baseline) had a significant treatment benefit; lesions in which the area of classic CNV was greater than 0% but less than 50% of the area of the entire lesion at baseline had **no visual acuity benefit** with treatment (i.e., no difference in the proportion of cases with a loss of ≥15 letters).

See id. at 1341, second column, first full paragraph (emphasis added).

Moreover, the additional features of the patient successfully treated using the claimed PDT are *not* identified in the TAP Report 1. The TAP Report 1 is completely silent regarding any additional feature that might be helpful in determining responsiveness to verteporfin PDT in patients with greater than 50% and less than 100% occult CNV. In categorizing the patients by visual acuity or area of the lesion, the character of the CNV lesions were **not** considered. The group of 305 patients treated with verteporfin include patients with <50% occult lesion (*i.e.*, ≥50% classical) *as well as* those with >0 to <50% classical CNV, *i.e.*, >50 to <100% occult CNV. Thus, in view of the numerous statements made by the TAP Report 1's authors that the patients with a CNV lesion with a significant occult character, a person of ordinary skill in the art would attribute the verteporfin-responsiveness to those patients having ≥50% classical CNV (less than 50% occult CNV).

Applicants respectfully submit that if the entirety of the TAP Report 1 is considered, it fails to render the claimed methods obvious. "A prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention." MPEP § 2141.03 (IV) (citation omitted)(original emphasis). The Examiner appears to be arguing that the treated group is inherently somewhere amongst the verteporfin-treated population because each of the three parameters were assessed *separately* in the TAP Report 1 whilst completely dismissing the express teachings of the TAP Report 1 that lesions between >50% and <100% occult

in character are non-responsive to verteporfin treatment. The assumption made by the Examiner is contradicted by actual data presented in the TAP Report 1 and its interpretation by its own authors. Moreover, the data presented in the instant application demonstrates that only unacceptably poor results can be achieved with the claimed method if the patients only are treated based on an occult lesion that is greater than 50% and less than 100% occult. *See* the specification at page 45, Table 2, 6th row. Nothing in the TAP Report 1 suggest selecting patients based on the claimed combinations of features to arrive at the beneficial results. The TAP Report 1 simply discloses that patients with >50% and <100% occult lesions cannot be successfully treated with verteporfin. Therefore, there cannot be a reasonable expectation of success in practicing the claimed methods.

In sum, the results shown in the specification demonstrate an unexpected and advantageous benefit in treating patients having CNV lesions that are greater than 50% and less than 100% occult as well as one or both of the claimed features of a lesion size of less than 5 disc areas and visual acuity of less than 65 letters prior to treatment.

For at least these reasons, the basis of this rejection may be removed.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. **273012012500**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: October 26, 2007

Respectfully submitted,

By _____

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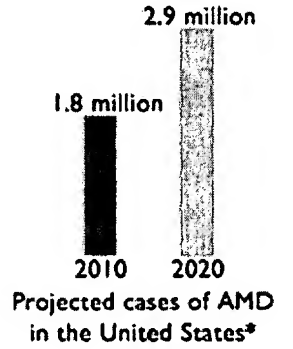
COMMERCIAL

About AMD

Age-related macular degeneration (AMD) is the major cause of vision loss in people over the age of 55. The early stage of AMD is characterized by fatty deposits on the back of the retina, called drusen. This form, known as dry AMD, is extremely common but is responsible for only 10% of the vision loss associated with the condition. It does however predispose a person to developing the more severe wet form of AMD, responsible for 90% of AMD vision loss and for which Visudyne® was developed to treat.

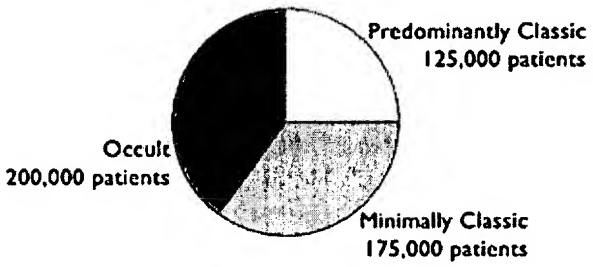
Wet AMD and North America's aging population
Over the next 20 years, as the population ages, the number of wet AMD cases is estimated to grow by 50%, according to the Eye Disease Prevalence Research Group. Affecting mainly Caucasians, this trend is creating a serious public health concern.



Projected cases of AMD in the United States*

*Archives of Ophthalmology, April 2004

Worldwide AMD Incidence
Worldwide there are 500,000 new cases of wet AMD each year, broken down in the graph to the right.

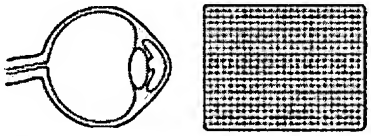


CNV caused by wet AMD appears as two types of lesions: classic or occult. These terms are used to describe different patterns of CNV leakage as seen on fluorescein angiography. Classic CNV progresses more rapidly than occult, is more aggressive and easier to diagnose because the vessels are well defined and therefore easier to detect. As well, loss of sight occurs more rapidly with classic CNV. Occult CNV is less predictable and, because the leakage is less obvious, it is more difficult to

diagnose. While it is common for patients to develop both types of lesions, roughly half of all patients with occult CNV will develop classic CNV within a year.

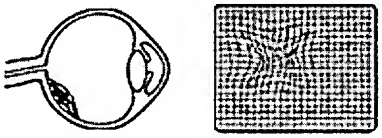
Classic AMD is broken down into two classifications: predominantly classic and minimally classic. Classic AMD lesions have more of a lacy appearance in the angiography than occult, which shows up as a more well-defined lesion. If more than 50% of the lesions are classic, it is referred to as predominantly classic. If there are less than 50% classic lesions in a patient, it is referred to as minimally classic.

Illustration of normal vision and vision with Age-related Macular Degeneration



healthy eye Amsler Grid

Healthy Eye: A healthy eye would show no development of abnormal blood vessels and would accurately observe the straight lines on the Amsler grid.



eye with AMD Amsler Grid

Eye with AMD: An eye with wet AMD develops abnormal blood vessels across the retina and would observe a distortion in the Amsler Grid.

Early detection is essential. The American Academy of Ophthalmology recommends patients see their eye care professional every year for a check up.

Deterioration of sight

Wet AMD is a devastating disease that causes a loss of central vision, resulting in a severe reduction in quality of life for patients as they lose their ability to read, watch television, drive, and even see the faces of their loved ones. It is caused by choroidal neovascularization (CNV), a growth of abnormal blood vessels under the central part of the retina, or the macula. These vessels leak fluid and cause scar tissue that attacks central vision, resulting in a deterioration of sight over a period that can range from a few months to three years.

Safe and well-tolerated

Visudyne therapy has also been shown to be safe and well-tolerated. The most frequently reported adverse events found

during clinical trials were injection site reactions and transient visual disturbances. Events leading to withdrawal from treatment were less than 4% and photosensitivity reactions occurred only 0.6% of the time.

Visudyne is a registered trademark of Novartis AG.

Last modified on April 30, 2007 at 04:32 PM.

QLT Inc.

Our business is science. Our product is life.